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PRINCIPAL INVESTIGATOR: Eva Balint, MD

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14. ABSTRACT This is a multidisciplinary postdoctoral award investigating the role of vitamin D in aromatase inhibitor-induced osteoporosis in breast cancer, supporting studies in basic science, clinical research and epidemiology.
During the reporting period, the recipient made significant progress in opening the clinical trial and progressing towards obtaining the MS degree in clinical epidemiology. The clinical trial received all necessary approvals including the IND from the FDA, and approvals from the IRB's from both at Stanford University and the DoD, and the trial is ongoing and recruiting participants.
The recipient is scheduled to graduate in the Fall quarter 2009, and is currently working on the master's thesis on the role of vitamin D in breast cancer in general, with a special focus on aromatase inhibitor-induced bone loss.
For the animal studies, the recipient obtained all necessary approvals for the experiments (Stanford University and DoD), and the studies will be performed during the third year.

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Introduction:

This is a multidisciplinary postdoctoral award investigating the role of vitamin D in aromatase inhibitor-induced osteoporosis in breast cancer. Building on the recipient's past experience in medicine, basic science and bone biology, the award supports the recipient's transition from basic science research towards establishing her as a successful new translational investigator in the breast cancer field. In order to achieve this goal, the award supports a basic science component (studies using an animal model), a prospective clinical trial and education toward a master's degree in the filed of epidemiology. The basic science component focuses on the effect of vitamin D on breast cancer and aromatase inhibitor-induced bone loss in an animal model. The clinical component is a randomized controlled prospective trial of vitamin D in preventing aromatase inhibitor-induced osteoporosis in breast cancer patients. The epidemiology component focuses on the role of vitamin D in breast cancer and aromatase inhibitor-induced osteoporosis, using methods of epidemiology, and the recipient is working towards obtaining a Master of Science (MS) degree in Clinical Epidemiology.

Key Research Accomplishments:

During the reporting period the recipient successfully negotiated a major barrier, access to fund due to Stanford University policy. As described in detail in the progress report submitted in January 2009 (for October 2008), funds for the entire award have not been released until October 2008. Because it is a violation of Stanford University policy and federal regulations to recruit, enter, follow subjects or analyze human subjects data unless the PI has IRB approval for the project, funds for the entire award has not been available until the protocol received Stanford IRB approval in October 2008. This hurdle resulted in delays in performing the animal studies, as well as taking classes for full credit in the Epidemiology Master's program. Since the release of funds, the recipient became a full member of the Stanford University community, able to take advantage of all the support necessary to run a clinical trial and prepare for graduation from the Master program in Clinical Epidemiology.

During the reporting period, the recipient successfully obtained approvals from Stanford's IRB, the DoD IRB and an IND from the FDA. The trial has been registered with Stanford University and Clinicaltrials.gov.
http://clinicaltrials.gov/ct2/show/NCT00904423
http://med.stanford.edu/clinicaltrials/publicCancerDisplayDetails.do?studyId=1302

The study drug has been manufactured and vitamin D content verified (Task 1). The trial has been opened and recruitment started (Task 5). The breast cancer oncologists at Stanford Cancer Center received the trial with enthusiasm and recommended participation to patients. Patients are identified relatively early during their primary treatment for breast cancer (neoadjuvant chemotherapy, surgery, chemotherapy or radiation therapy, oophorectomy). Because of the early identification, most patients are actively followed for several weeks, or even months before enrollment. We established good relationships with all breast cancer oncologists who became collaborators in the trial and referring their patients (please see attached brochure). We screened over 1200 patient visits to identify candidates (please note that patients might have had multiple

visits during this time period). To date, five patients signed informed consent and undergone eligibility screening, including bone mineral density testing, blood and urine tests. Three patients have been randomized and currently taking the study drug. We are currently following about 20 patients who will meet eligibility criteria within the next weeks or months (starting an aromatase inhibitor for a non-metastatic estrogen receptor positive breast cancer). The protocol has been modified and prepared for re-submissions to the IRB to streamline the inclusion and exclusion criteria and facilitate recruitment. Continuing renewal has been approved by Stanford IRB and has been recently submitted to the DoD HRPO for continuing review.

As far as the animal studies, the recipient obtained all necessary approvals for the experiments (both from Stanford University and the DoD), and the yearly renewal has been satisfied as well. As the funds have not been available, the actual studies have been delayed and will be performed during the third year of the award (task 2).

The recipient completed all the courses necessary to meet graduation requirements for the Master's degree in Epidemiology, and is expected to graduate in the Fall Quarter 2009 (Task 7). The recipient is currently working on the master's thesis on the role of vitamin D in breast cancer in general, with a special focus on aromatase inhibitor-induced bone loss. The thesis will be submitted with the upcoming progress report in October 2010.

Reportable Outcomes:

The award recipient presented a poster at the Leading Innovation and Knowledge Sharing (LINKS) meeting in Vienna, VA, February 9-10, 2009.

Conclusions:

The recipient of this multidisciplinary postdoctoral award successfully made the transition from basic science physician-scientist towards becoming a clinical and translational research investigator. Despite the challenges, she successfully opened the clinical trials and is currently recruiting participants. Approvals have been obtained for the animal studies as well, and the studies will be performed during the third year of the award. The recipient completed all courses necessary to meet graduation requirements for the master's degree in epidemiology to graduate in the Fall quarter 2009, and currently working on the master's thesis in the field of vitamin D and breast cancer.

References:

N/A

Appendix:

Study brochure (please see attached)

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For additional information about breast cancer research at Stanford Comprehensive Cancer Center please visit
http://cancer.stanford.edu

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STANFORD
SCHOOL OF MEDICINE
Stanford University Medical Center

A Phase I/II randomized, double-blind, controlled study to evaluate efficacy and safety of vitamin D on bone mineral density and markers of bone resorption in aromatase inhibitor-induced bone loss in women with breast cancer.

Examining the effect of vitamin D on bone loss associated with aromatase inhibitors

A research project for women receiving therapy to reduce recurrence of breast cancer

Funded by
US Department of Defense,
Breast Cancer Research Program

Tel: 650-498-7977

How Can You Become Involved

We invite you to participate in our study of vitamin D and breast cancer. This study is funded by the US Department of Defense, Breast Cancer Research Program and is being conducted at Stanford University Medical Center.

Our Goals

The purpose of this study is to investigate the effect of vitamin D on bone loss associated with a group of medications called aromatase inhibitors, given for the prevention of breast cancer recurrence.

Benefits Of Participation

There may be no benefit to you from participating in this study. Your participation will provide us with valuable information that may be used to develop improved therapies for preventing breast cancer recurrence.

What Will Be Asked Of You

- Donate 1 tablespoon of blood and urine sample on 4 different occasions
- Have your bone density measured on 2 occasions
- Take vitamin D by mouth for one year
- That you allow us to access your medical record to collect information about your medical history and characteristics of your breast cancer.

Contact Information

If you are interested in participating or finding out more about this study please call:

Charlene Kranz
Project Research Coordinator
650-498-7977
Email: ckranz@stanford.edu

Who Is Eligible To Participate?

We are recruiting women who have had breast cancer and completed their primary surgical and/or chemotherapy and who are candidates to take medication called aromatase inhibitors to reduce recurrence of breast cancer.

Women are not eligible if they have severe bone loss (osteoporosis), have increased calcium or parathyroid hormone in their blood, have a history of kidney stones or have an intestinal problem that interferes with the absorption of vitamin D, or if they are known to be pregnant or are breast feeding.

For further information regarding questions, concerns or complaints about research, research related injury, and questions about the rights of research participants, please call (650)723-5244 or tool free 1-866-680-2906 or write the Administrative Panel on Human subjects in Medical Research, Administrative Panels Office, Stanford University, Stanford, CA 94305-5401